REMARKS

This Preliminary Amendment is submitted in advance o/f the first substantive examination of the subject application. Claims 1-12 were pending prior to this communication. By the present communication, new claims 13-15 have been added, claims 4 and 5 have been cancelled without prejudice, and claims 1, 6, and 12 have been amended to define Applicant's invention with greater particularity. Support for the amendments to claim 1 is provided by original claims 4 and 5 and support for the amendment to claim 12 is provided in Examples 8-10 at pages 41-43 of the specification. Support for new claim 13 is provided at page 9, lines 15-27, at page 10, line 24 to page 21, line 31, and at pages 34-35 (Example 2). Support for new claims 14 and 15 is provided in the Specification at page 30, line 30 to page 32, line 36 and pages 35-45 (Examples 3-13). Thus, the amendments add no new matter, being fully supported by the Specification and original claims. Accordingly, claims 1-3 and 6-15 are currently pending.

THE RESTRICTION REQUIREMENT

In response to the Requirement for Restriction mailed November 4, 2003, Applicant elects, with traverse, Group VI consisting of Claims 1 and 3-7, drawn to an adjuvant that comprises a natural bacterial toxin, specifically cholera.

However, Applicant traverses the restriction requirement as applied to the claims as amended herein. Since the instant application was filed under Rule 371, the PCT rules regarding "unity of invention" apply. PCT Rule 13.2 stipulates that the requirement of unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding "special technical features." The expression "special technical features" is defined as those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art.

I. The technical feature of this invention provides a contribution over the prior art.

The Examiner asserts that the thirty groups of inventions set forth in the Restriction Requirement are not so linked as to form a single general inventive concept under PCT Rule 13.1. As support for this assertion, the Examiner has cited WO 95/32737, which recites a use of an attenuated Clostridial toxin as a transporter, and concludes that the technical feature of the present invention, namely an attenuated toxin, does not provide a contribution over the prior art.

However, claim 1, as amended herein, recites specific toxins (listed in original claim 5) having specific features that are not disclosed or suggested in the cited art, WO 95/32737, namely the adjuvant, toxic activity and bacterial species. Moreover, attenuated toxins retains glutamic acid residues of their natural amino acid sequences are not disclosed in WO 95/32737. For example, inactivated Clostridial neurotoxins disclosed by the reference include those having a modification at a position of a glutamic acid residue in the corresponding natural amino acid sequences (WO 95/32727 page 2, lines 28-31). Since the reference fails to disclose any of the specific features recited in the present invention, as defined by amended claim 1, Applicant believes that WO 95/32727 is not sufficient to break the unity of invention for the present claims. The special technical feature, an attenuated toxin, is also common to new claims 13-15. Therefore, Applicant requests rejoinder of Groups I through XXX, including new claims 13-15, for prosecution in a single application.

II. The Examiner improperly applies the administrative rules to the Markush claim.

MPEP stipulates regarding Markush practice as follows:

> If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner *must* examine all the members of the Markush group in the claim on the merits, *even though* they are directed to independent and distinct inventions. In such a case, the examiner . . . will not require restriction.

(MPEP 803.02; emphasis added). Amended claim 1 incorporates the Markush group from original claim 5, which recites only five specific toxins as members of the group, each directed to a related-attenuated toxin and all functioning as adjuvants.

In addition, the administrative rules governing Markush practice consider members of a "similar nature" as suitable for grouping together:

> [t]he situation involving the so-called "Markush practice" wherein a single claim defines alternatives (chemical or non-chemical) is also governed by Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the *alternatives are of a similar nature.*

(MPEP Appendix AI, Annex B; emphasis added). The MPEP considers compounds as being of a similar nature when (i) all alternatives in the group have a common property or activity; and (ii) all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains. Applicant submits that here the phrase "recognized class of chemical compounds" means that those of skill in the art would expect based on knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member of the group can be substituted for another, with the expectation that the same intended result would be achieved. Similarly, although the toxins in the group listed are structurally distinct, they all have a common property; all would function as adjuvants to enhance antibody production. Also, substitution of one adjuvant for another in the group would still have the same intended result. Therefore, Applicant respectfully submits that the Examiner has improperly applied the administrative rules, as defined in MPEP, Appendix AI, Annex B, to Applicant's Markush claim.

III. Unity of invention is considered only in relation to the independent claims.

The administrative rules also state that unity of invention is considered only in relation to the independent claims, and not the dependent claims:

> Unity of invention has to be considered in the first place *only in relation to the independent claims* in an international application and not the dependent claims. By "dependent" claims is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression "category of claim" referring to ...). If the independent claims avoid the prior art and satisfy the requirement of unity of invention, *no problem of lack of unity* arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention.

(MPEP, Appendix A1, Annex B, Part I; emphasis added) In the present case, Applicant respectfully submits that the Examiner has clearly ignored the administrative instructions regarding treatment of dependent claims. In this application there is only one independent claim, namely, claim 1. All other claims are in dependent form. For this reason alone, Applicant submits that the restriction of claims is flawed and Applicant respectfully requests rejoinder of claims 1-3 and 6-15 (Groups I through XXX) for prosecution in this application.

If the Examiner would like to discuss this response, please contact the Applicants' representative noted below.

Respectfully submitted,

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